

## CORRESPONDENCE



# Vasopressor weaning in septic shock: the missing piece in the 2026 guidelines

Cássio Mallmann<sup>1,2,3\*</sup> , Wagner Luis Nedel<sup>1,2,3</sup> , Rafael Barberena Moraes<sup>1,2,4</sup> and Gilberto Friedman<sup>1,2</sup>

© 2026 Springer-Verlag GmbH Germany, part of Springer Nature

We have reviewed with considerable interest the recent guidelines from the Surviving Sepsis Campaign (SSC) [1]. While these guidelines offer comprehensive recommendations on the initiation and escalation of vasopressors, they do not address a common clinical challenge: the safe de-escalation of vasopressors during the stabilization phase. Notably, in 2024, the SSC identified vasopressor weaning as a research priority, specifically highlighting uncertainties regarding the sequence of discontinuation and the optimal strategy for vasopressin withdrawal. In 2018, Jeon et al. [2] published the first randomized clinical trial (RCT) on this topic—the DOVSS study—which reported a higher incidence of hypotension when weaning was initiated with norepinephrine, contrasting with findings from previous observational studies. Importantly, the DOVSS study employed a protocolized titrated reduction of vasopressin, whereas most observational studies utilized abrupt discontinuation without dose titration. The RENOVA trial [3], published in 2025, corroborates the findings of Jeon et al. Although no formal protocol for vasopressin weaning was implemented, vasopressin was reduced in a titrated manner in 92% of cases. RCTs indicate a higher incidence of hypotension when norepinephrine is withdrawn first, challenging previous findings based on observational studies. Collectively, these findings suggest that the observed divergence may be partially explained by differences in the method

of vasopressin withdrawal—specifically, titrated reduction versus abrupt discontinuation (Fig. 1).

To date, only two studies have specifically compared vasopressin withdrawal strategies—both observational [4, 5]—and neither identified differences in the incidence of hypotension. Notably, in the Murata cohort, norepinephrine had already been discontinued at the time of vasopressin withdrawal. Given the limited evidence on this topic, we are currently conducting a randomized clinical trial (NCT07067866) to compare vasopressin withdrawal strategies during the stabilization phase of septic shock. Endogenous vasopressin levels increase early in septic shock but rapidly decline within 48 h, resulting in a state of relative vasopressin deficiency, which may have implications for the timing and strategy of vasopressor withdrawal. Assessing endogenous vasopressin release may be useful in predicting hypotension following the discontinuation of exogenous vasopressin. However, direct measurement of vasopressin is technically challenging. Copeptin, a stable surrogate of vasopressin release, has emerged as a potential predictor of hypotension following vasopressin discontinuation, although its role in clinical decision-making remains uncertain.

Since the 2021 Surviving Sepsis Campaign guidelines, evidence on vasopressor weaning has expanded. Although conclusive data are still lacking—similar to other areas addressed by the guidelines—available evidence may support bedside decision-making in this frequently encountered clinical scenario. The de-resuscitation phase remains underexplored, and recognition of these gaps may foster the development of future studies. In this issue of SSC, active fluid removal has already

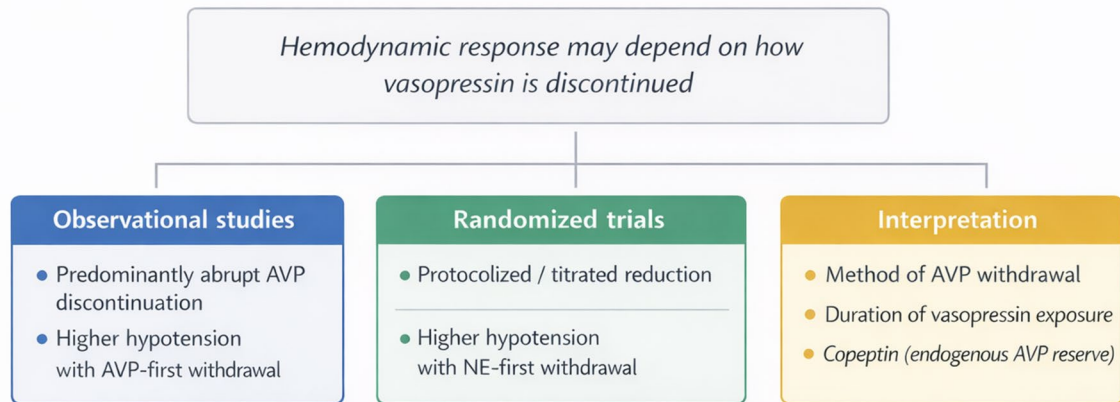
\*Correspondence: [cassiomallmann@hcpa.edu.br](mailto:cassiomallmann@hcpa.edu.br)

<sup>1</sup> Postgraduate Program in Pulmonary Sciences, Federal University of Rio Grande do Sul (UFRGS), Porto Alegre, Brazil  
Full author information is available at the end of the article

**SHOUT**  
**SHARE** **IT**



## Vasopressor weaning in septic shock: conflicting evidence



*Abrupt AVP discontinuation may increase **hemodynamic instability**.*

**Fig. 1** Conflicting evidence on vasopressor weaning in septic shock. Observational studies report a higher incidence of hypotension with vasopressin-first withdrawal, whereas randomized trials report a higher incidence with norepinephrine-first withdrawal

received a recommendation. This is a step forward in the discussion of therapy withdrawal in septic patients. We hope this topic will be extended to vasopressor management in future issues of SSC.

### Author details

<sup>1</sup> Postgraduate Program in Pulmonary Sciences, Federal University of Rio Grande do Sul (UFRGS), Porto Alegre, Brazil. <sup>2</sup> Critical Care Unit, Hospital de Clínicas de Porto Alegre, Porto Alegre, Brazil. <sup>3</sup> Critical Care Unit, Hospital Nossa Senhora da Conceição, Porto Alegre, Brazil. <sup>4</sup> Critical Care Unit, Hospital Fêmina, Porto Alegre, Brazil.

### Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

### Declarations

### Conflicts of interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

### Publisher's Note

Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.

Received: 1 April 2026 Accepted: 6 April 2026

Published online: 13 April 2026

### References

1. Prescott HC, Antonelli M, Alhazzanic W, Möller MH, Alshamsi F, Azevedo LCP et al (2026) Surviving Sepsis Campaign: international guidelines for management of sepsis and septic shock 2026. *Intensive Care Med.* <https://doi.org/10.1007/s00134-026-08361-1>
2. Jeon K, Song JU, Chung CR, Yang JH, Suh GY (2018) Incidence of hypotension according to the discontinuation order of vasopressors in the management of septic shock: a prospective randomized trial (DOVSS). *Crit Care* 22(1):131. <https://doi.org/10.1186/s13054-018-2034-9>
3. Mallmann C, Galiotto TMB, de Oliveira MS, Moraes RB (2025) Reduction of norepinephrine versus vasopressin in the stabilization phase of septic shock: RENOVA clinical trial. *Med Intensiva (Engl Ed)* 49(10):502147. <https://doi.org/10.1016/j.medine.2025.502147>
4. Lam SW, Sacha GL, Duggal A, Reddy AJ, Bauer SR (2021) Abrupt discontinuation versus down-titration of vasopressin in patients recovering from septic shock. *Shock* 55(2):210–214. <https://doi.org/10.1097/SHK.0000000000001609>
5. Murata J, Buckley M, Lehn J, Agarwal SK, Stevenson B, Martinez B et al (2023) Incidence of hypotension associated with two different vasopressin discontinuation strategies in the recovery phase of septic shock. *J Pharm Pract* 36(4):830–838. <https://doi.org/10.1177/08971900221078270>